

Con la colaboración de



Dermatitis atópica y Psoriasis ¿Diferentes espectros de una misma realidad?

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Germans Trias i Pujol
Hospital

**Inmunoterapia
en dermatología**

V EDICIÓN

Conflictos de interés

Investigador, speaker, y advisor para: AbbVie, Almirall, Amgen, Boehringer Ingelheim, Celgene, GSK, Eli Lilly, Galderma, Janssen, LEO Pharma, Novartis, UCB



Psoriasis vs Dermatitis atópica



Psoriasis

- Prevalencia del 2.3% de la población
- Más prevalente en la edad adulta temprana
- 90 % de psoriasis en placas



Dermatitis atópica

- 15-20% a lo largo de la vida.
- Es más frecuente en la infancia, pero también es común en adultos.
- Heterogeneidad clínica/genética/fenotípica.

Psoriasis vs Dermatitis atópica



Hospital Psoriasis



Dermatitis Atópica

Psoriasis vs Dermatitis atópica

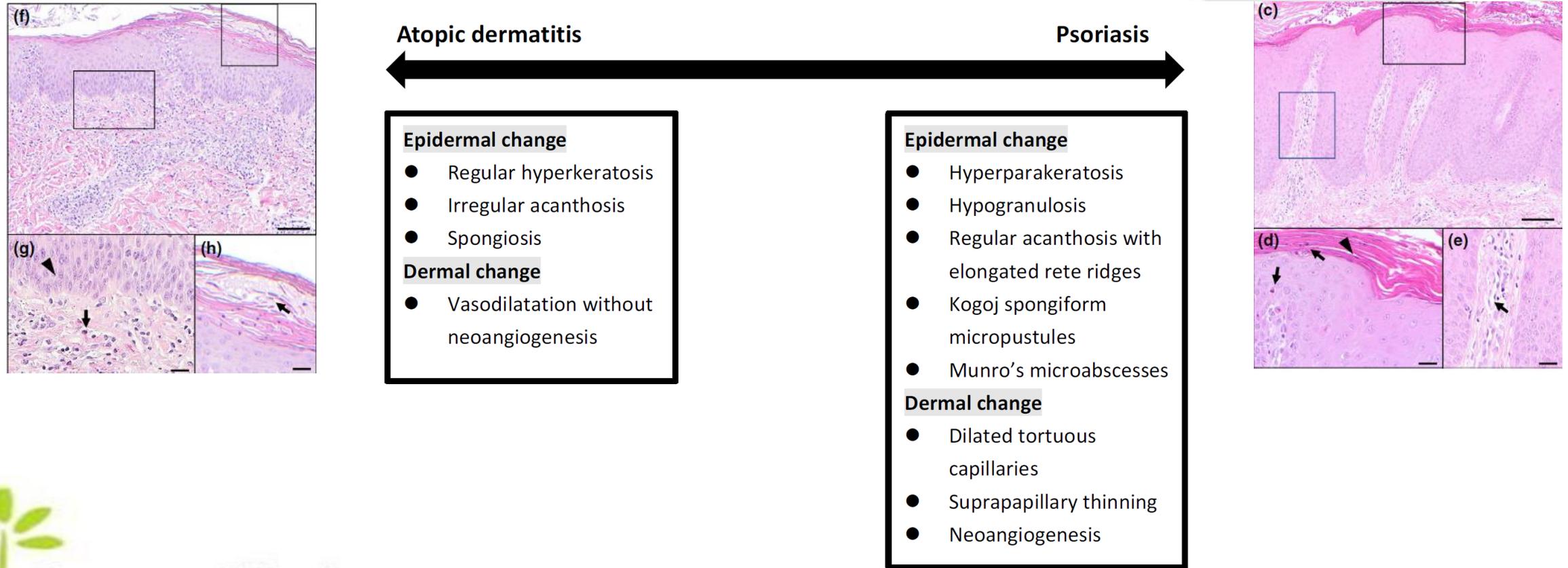
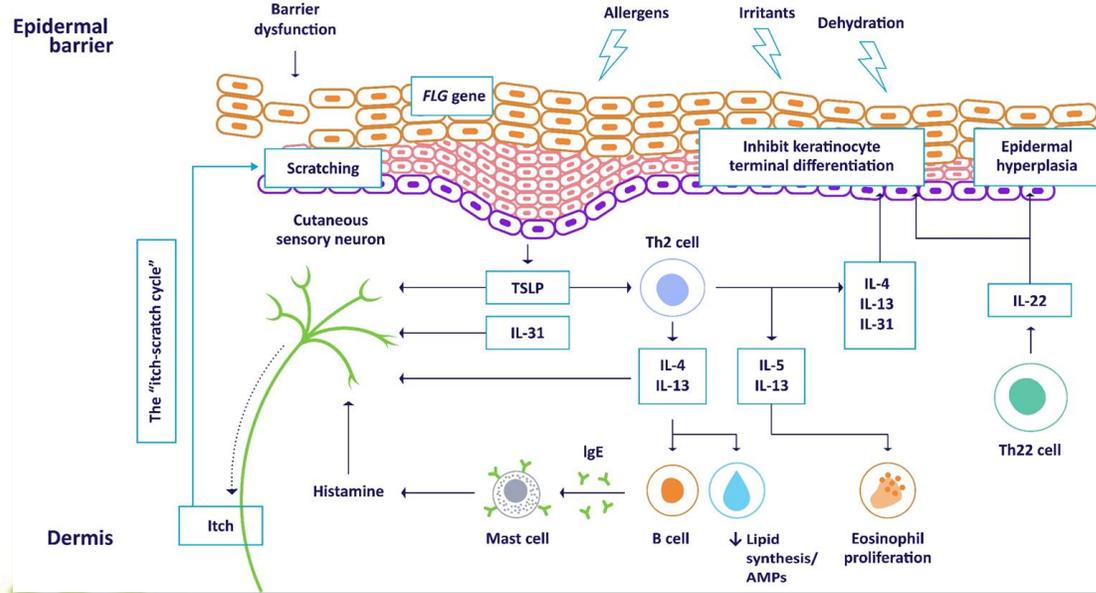


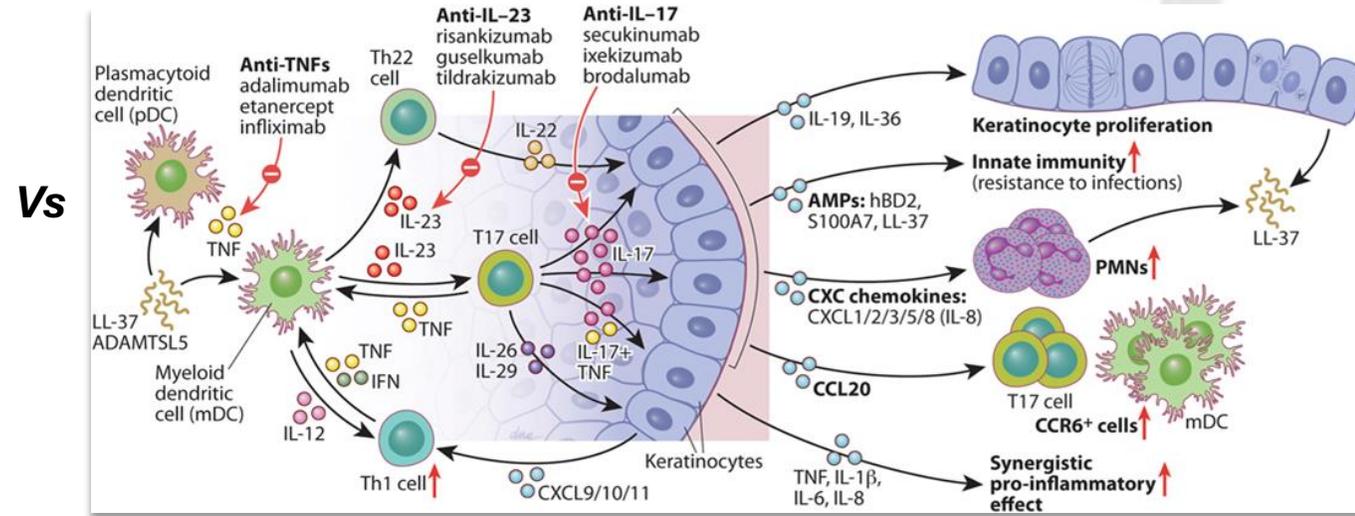
Figure 3. Histopathologic change in between atopic dermatitis and psoriasis.

Psoriasis vs dermatitis atópica

Dermatitis Atópica Th2/ IL4



Psoriasis IL23/ IL17





Psoriasis

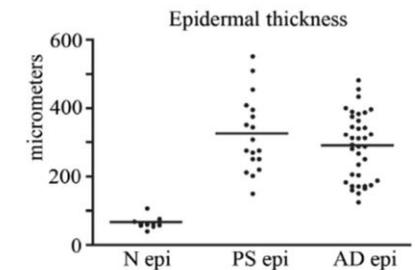
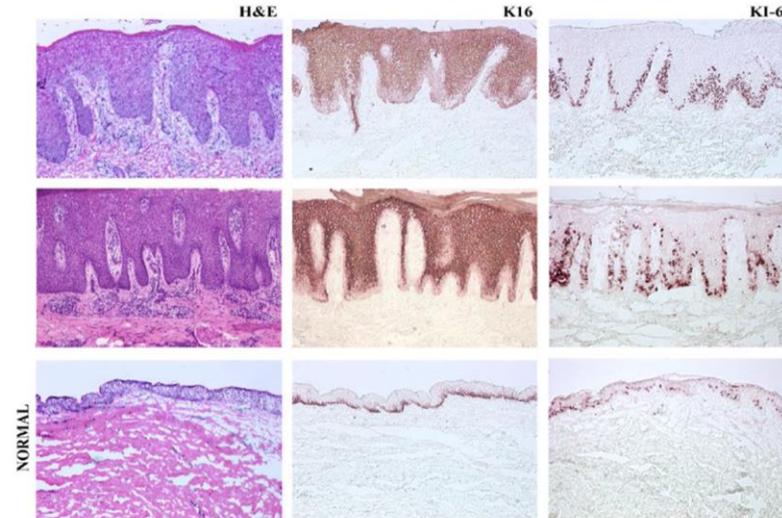


Dermatitis atópica



Psoriasis y DA: 2 enfermedades de la piel "bajo el mismo paraguas"

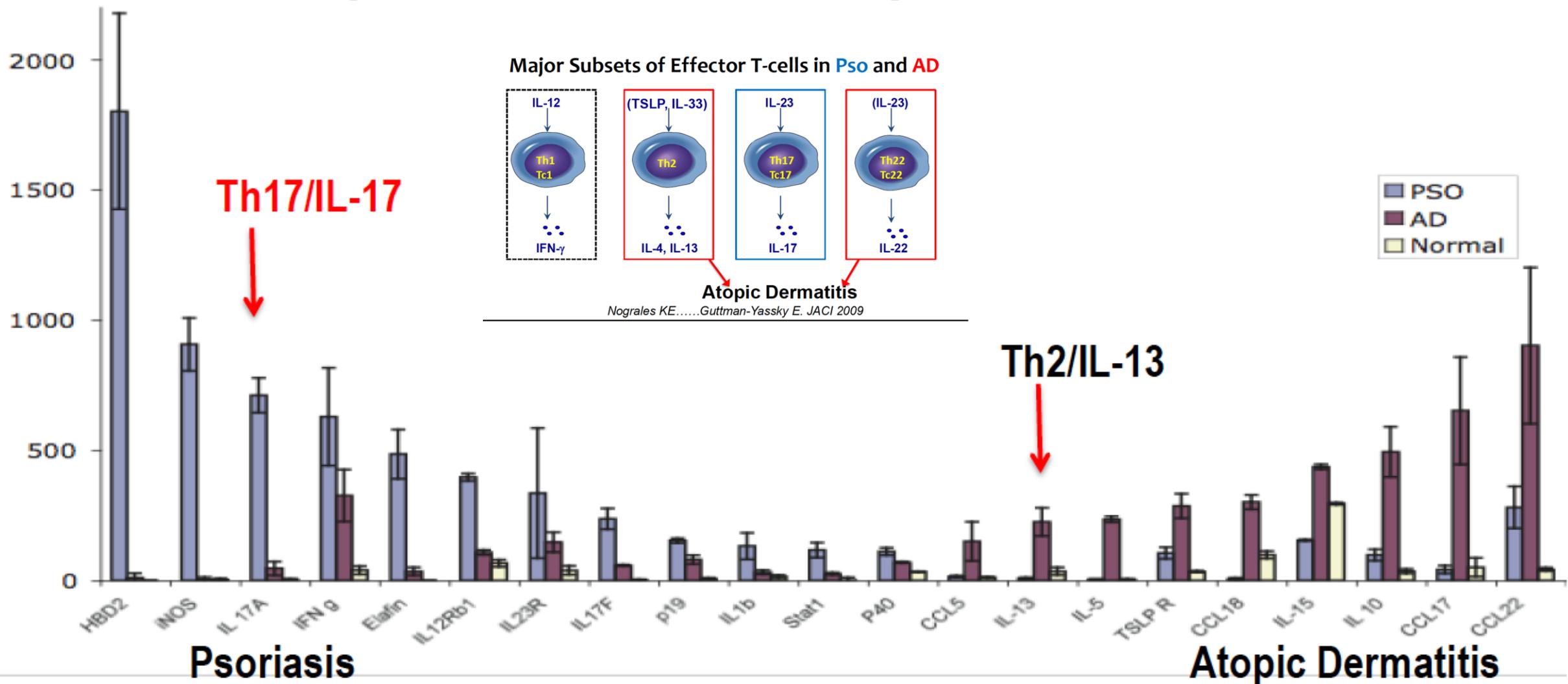
- La dermatitis psoriasiforme se puede utilizar como término general para describir tanto la psoriasis vulgar como la dermatitis atópica crónica
- A nivel mecanicista, ambas dermatosis podrían clasificarse como respuestas de hiperplasia epidérmica a citoquinas producidas por **células T activadas en lesiones cutáneas**



Guttman-Yassky et al. J Allergy Clin Immunol 2007

Concept by Krueger

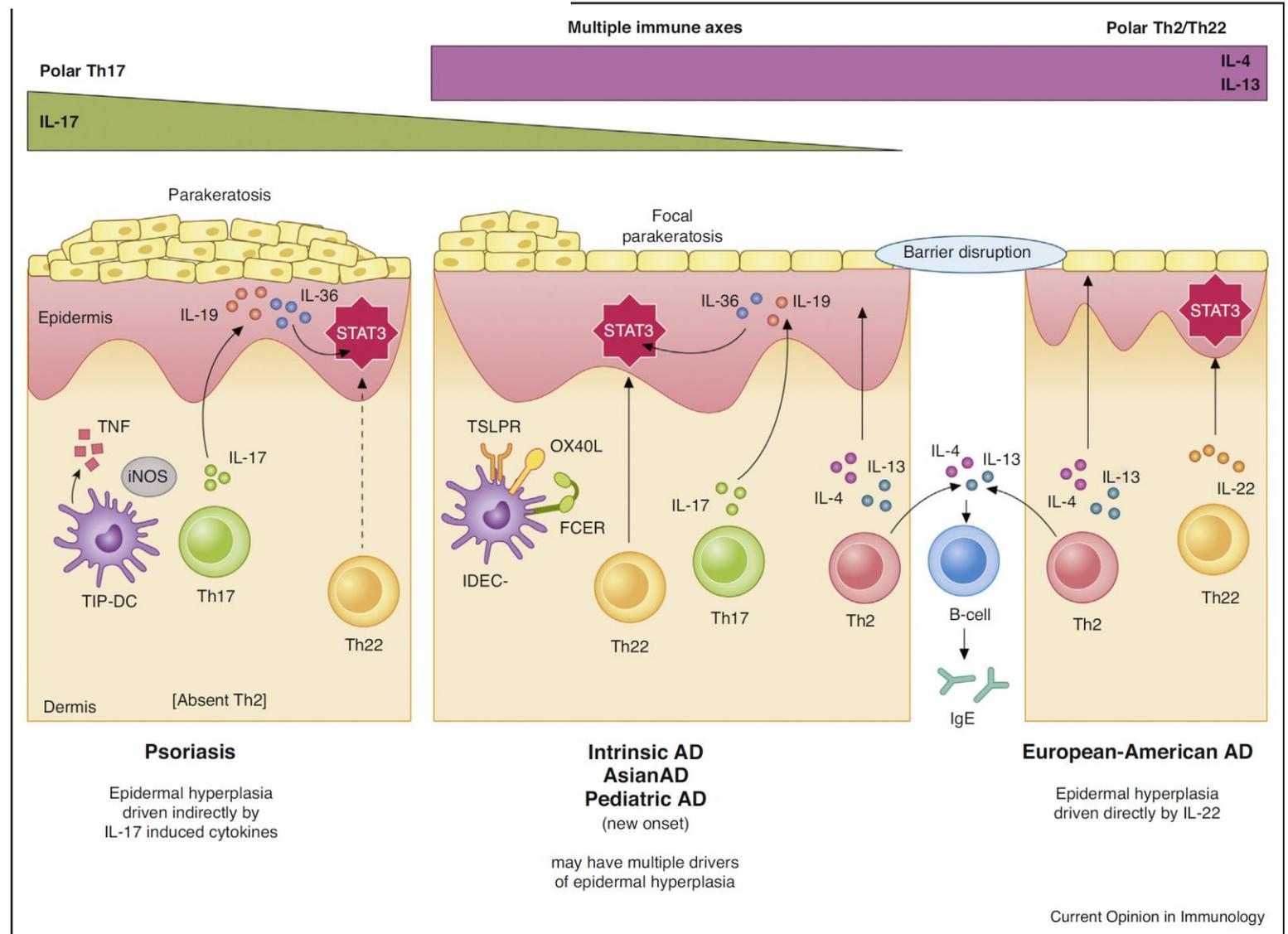
View of psoriasis and AD as “polar” immune diseases



Guttman-Yassky E...Krueger JG. J Immunol 2008

Psoriasis vs dermatitis atópica

- El eje Th17 de la EA europeo-americana está regulado a la baja en adultos con EA extrínseca
- La EA asiática es una enfermedad con características tanto de psoriasis como de EA-AD, así como de una fuerte activación de las células T Th2, Th17 y Th22 en lesiones cutáneas
- Características similares en la EA intrínseca, la EA asiática y la EA pediátrica



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ScienceDirect

Current Opinion in
Immunology

Atopic dermatitis and psoriasis:
two different immune diseases
or one spectrum?

Emma Guttman-Yassky¹ and James G Krueger²



Overlapping Pso-AD



THIS IS A BEFUNKY PLUS FEATURE.



Superposición de Pso-AD

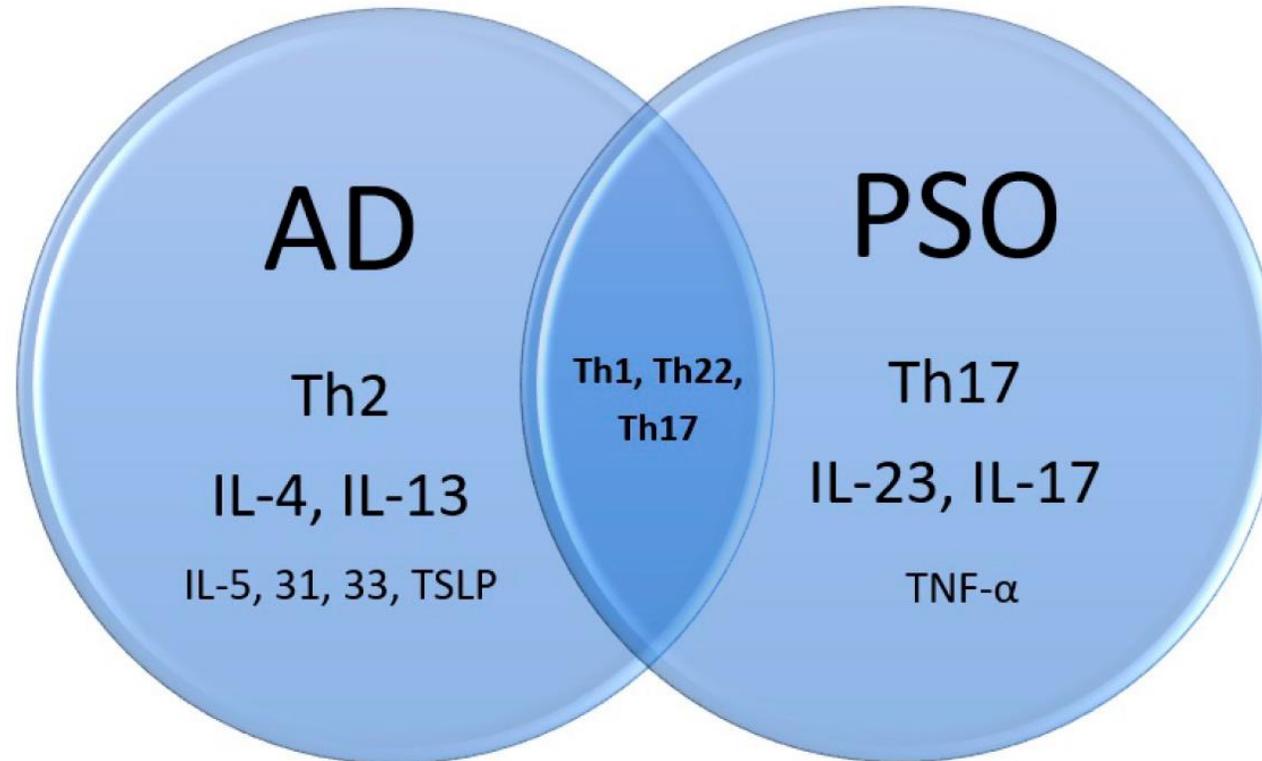


Figure 2. Immunopathogenesis of atopic dermatitis, psoriasis, and the overlap.

Review

Overlapping Features of Psoriasis and Atopic Dermatitis: From Genetics to Immunopathogenesis to Phenotypes

Ya-Chu Tsai ¹ and Tsen-Fang Tsai ^{2,*} 

Int. J. Mol. Sci. 2022, 23,
5518. [https://doi.org/10.3390/
ijms23105518](https://doi.org/10.3390/ijms23105518)

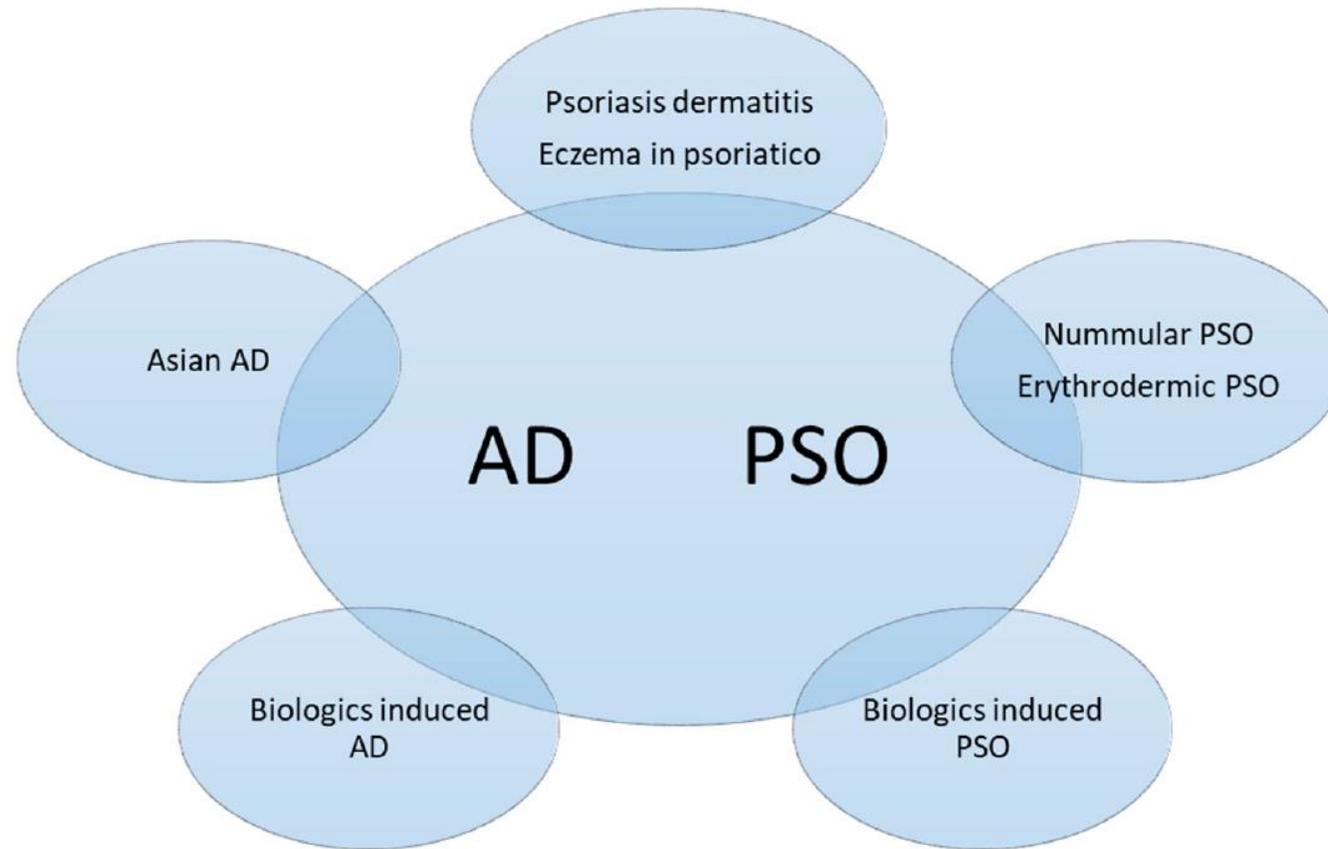


Superposición de Pso-AD

- **Borderland psoriasis – atopic dermatitis**
- Variantes superpuestas Pso-AD: psoriasis dermatitis
- Variantes dinámicas
- Reacciones psoriasiformes bajo terapias con IL4/13
- Reacciones eccematosas bajo terapias antiTNF/IL-17
- Erupciones inespecíficas
- Implicaciones terapéuticas



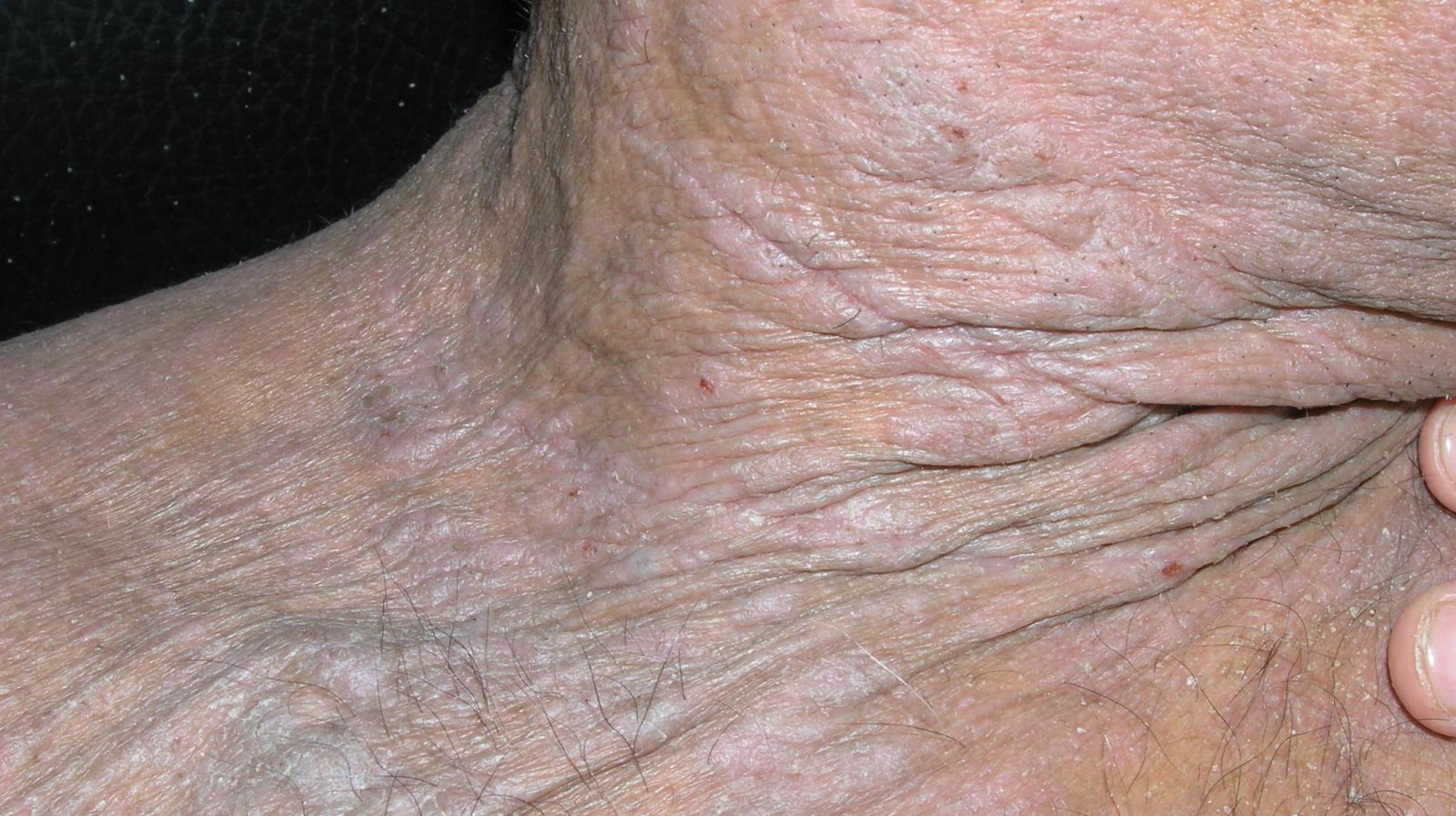
“the borderland” PSO-AD



AD de tipo asiático

- Aumento de la acantosis, niveles más altos de Ki-67 y más paraqueratosis que EA-AD, junto con hipogranulosis y elongación de las crestas de la red.
- La **infiltración de neutrófilos** es más común en la EA asiática que en la EA-AD, lo que se alinea con una característica típica de la PSO.
- Tanto la EA asiática como la EA-AD **tienen citocinas dominantes Th2 (IL-4 e IL-13)**, pero la EA asiática muestra de manera única una activación robusta de las **citocinas relacionadas con Th17 y Th22 (IL-17, IL-19, IL-22)**, lo que conduce a una hiperplasia epidérmica prominente.





Eczema
numular



o psoriasis numular?



SAGLB DU.P.19.10.1481 October 2019

Overlapping Pso-AD

- Borderland psoriasis – atopic dermatitis
- **Variantes superpuestas Pso-AD: psoriasis dermatitis**
- Implicaciones terapéuticas
- Variantes dinámicas
- Reacciones psoriasiformes bajo terapias con IL4/13
- Reacciones eccematosas bajo terapias antiTNF/IL-17
- Erupciones inespecíficas



Psoriasis-dermatitis

- Presencia de lesiones de psoriasis (PSO) y dermatitis atópica (DA) en el mismo individuo, conocidas de forma variable como "**síndrome de superposición PSO-AD**", "enfermedad concomitante de PSO y EA", etc.
- **Más lesiones faciales y menor afectación del cuero cabelludo**, con cambios en las uñas comparables a los de los pacientes con psoriasis.
- Durante una mediana de seguimiento de 1,2 años, los síntomas de la EP **persistieron sin un diagnóstico claro de EA o psoriasis**; solo un paciente fue finalmente diagnosticado con EA.



Psoriasis dermatitis

- A menudo requiere tratamientos biológicos múltiples o consecutivos, lo que indica su naturaleza recalcitrante y complejidad.
- Los niveles de IL-17 son significativamente más altos en la EP que en la EA o la PSO solas, lo que enfatiza el papel del eje Th17.



Perfil de las variantes overlap de Pso-AD

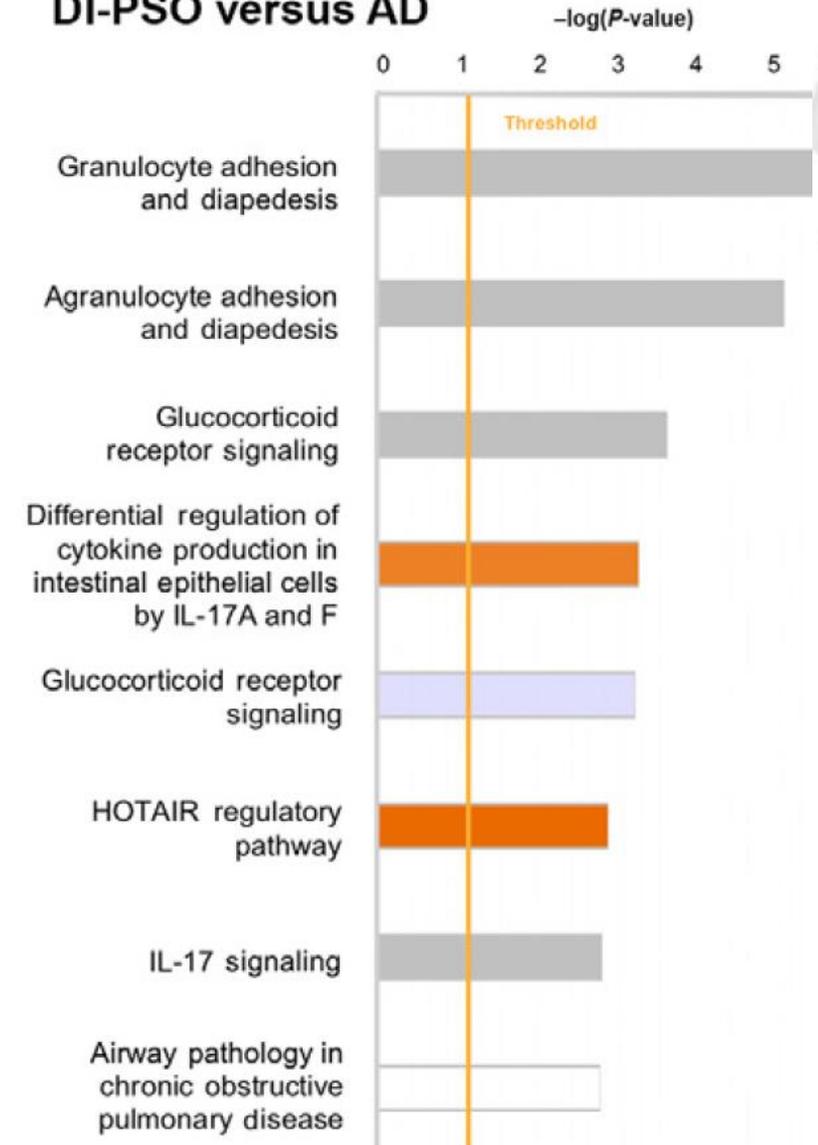
- Análisis comparativo con psoriasis en placas, dermatitis atópica y controles sanos.
- El AD-Pso se caracteriza por la **activación de las vías T helper 17/IL-23 y una alta expresión de IL-36**, un marcador de psoriasis pustulosa.
- **Marcada disminución en la expresión de los genes de barrera cutánea**, lo que indica cambios profundos en las funciones de barrera cutánea en DI-Pso.

IL-4/IL-13 Inhibitors for Atopic Dermatitis Induce Psoriatic Rash Transcriptionally Close to Pustular Psoriasis

Chloé Grolleau^{1,2}, Andreea Calugareanu^{2,3}, Sarah Demouche^{1,2}, Audrey Nosbaum³, Delphine Staumont-Sallé⁴, Hélène Aubert⁵, Charles Cassius^{1,2}, Marie Jachiet¹, Anne Saussine¹, Martine Bagot¹, Hervé Bachelez^{1,6}, Maxime Battistella⁷, Claire Hotz⁸, Aurélie Du Thanh⁹, Marie-Noëlle Crépy¹⁰, David Bergerat², Marine Merandet², Rachel Onifarasoiaina¹¹, Antonio Alberdi¹², Alexandre How-Kit¹³, Jean-David Bouaziz^{1,2} and Hélène Le-Buanec²

J Invest Dermatol. 2023 May;143(5):711-721.e7. doi: 10.1016/j.jid.2022.10.015

DI-PSO versus AD



Z-score=0 ■ No activity pattern available



Hospital

Psoriasis patient treated with anti IL-17 inhibitor

Paradoxical eczematous reaction to ixekizumab

Editor

A 31-year-old man with severe psoriasis treated with ixekizumab presented with a 1-month history of pruritic lesions. The patient had no personal or family history of allergy, atopic dermatitis or eczema, and he reported no recent medication changes. Medical history was significant for plaque psoriasis diagnosed at age 10. Previous therapies included topical steroids, phototherapy and cyclosporine, none of which were effective. Treatment with ixekizumab, started 14 months before the episode, achieved an almost complete response of his skin disease.

significantly decreased. Those relatively lower levels of IL-17 may explain the deficiency of antimicrobial peptides produced by keratinocytes, which increases the rate of bacterial infections, such as *S. aureus*.⁸ Although our patient had no personal or family history of atopy, total and specific IgE were increased, with uncertain clinical significance. It could be hypothesized that, in predisposed patients, IL-17 inhibition may favour the development of eczema-like inflammation in psoriatic areas. Moreover,



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- Implicaciones terapéuticas

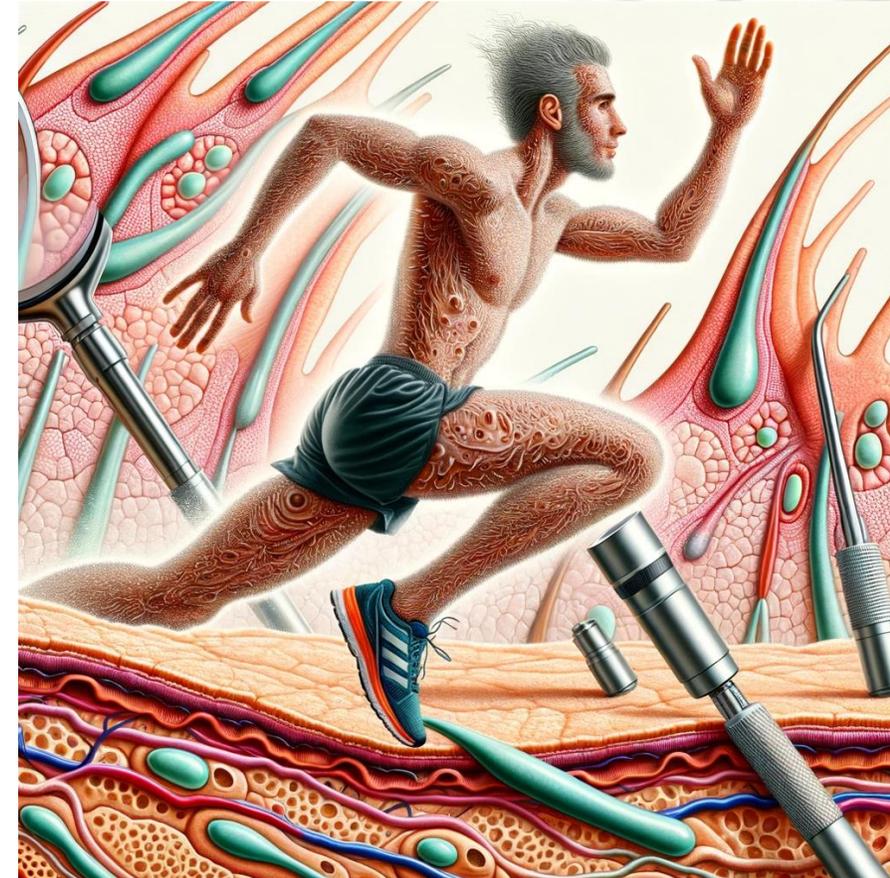


Image created with Dall-E @jmcarrascosa

Reacciones eccematosas con fármacos anti IL17

- Erupciones inflamatorias cutáneas en pacientes psoriásicos tratados con agentes anti IL-17A, secukinumab o ixekizumab.
- Análisis retrospectivo de 468 pacientes, con revisión sistemática de la literatura de casos similares.
- El 5,8% de los pacientes desarrollaron erupciones (eccema agudo, erupción similar a la dermatitis atópica o erupción psoriasiforme) después de un promedio de 17 semanas.
- Todos los casos presentaron espongiosis epidérmica, lo que indica inflamación.



Clinical and histopathological characterization of eczematous eruptions occurring in course of anti IL-17 treatment: a case series and review of the literature

G. Caldarola^{ab}, F. Pirro^{ab}, A. Di Stefani^{ab}, M. Talamonti^c, M. Galluzzo^c, S. D'Adamio^c, M. Magnano^d, N. Bernardini^e, P. Malagoli^f, F. Bardazzi^d, C. Potenza^e, L. Bianchi^c, K. Peris^{ab} and C. De Simone^{ab}

Reacciones eccematosas ... no sólo con fármacos anti Il17

In summary, trial data comprising 17 367 patient-years demonstrated that the overall frequency of eczematous reactions was low across the treatments, and no statistically significant differences were noted between IXE, ETN and UST. The events were generally mild in nature, appeared more often in patients with a history of eczema, and rarely led to treatment discontinuation.



P.M. Brunner ¹, C. Conrad,² R. Vender ³, S. Grond,⁴
C. Schuster,^{1,4} H. Patel,⁴ W. Xu⁴ and J.M. Carrascosa Carrillo⁵

Integrated safety analysis of treatment-emergent eczematous reactions in patients with moderate-to-severe psoriasis treated with ixekizumab, etanercept and ustekinumab

DOI: 10.1111/bjd.20527

Paciente atópica tratada con inhibidor anti IL-4/13



Exacerbación psoriasiforme después de 6 semanas de tratamiento con dupilumab



Germans Trias i Pujol

<https://doi.org/10.1016/j.ad.2023.04.025>

REVISIÓN

Inhibidores de JAK en dermatitis atópica, nuevas perspectivas

M. Munera-Campos* y J.M. Carrascosa

Reacciones psoriasiformes con terapias anti IL4

- Se revisaron 39 publicaciones en las que participaron 112 pacientes con dermatitis atópica tratados con dupilumab.
- 101 desarrollaron psoriasis "de novo" y 11 experimentaron brotes de psoriasis.
- La mayoría de los pacientes presentaban psoriasis en placas en cuero cabelludo y extremidades.
- La psoriasis "de novo" apareció típicamente 5 meses después del tratamiento; El 43% de los pacientes con psoriasis existentes tuvieron brotes dentro de los 4 meses.
- La interrupción del dupilumab condujo a una mejoría de la psoriasis en el 38% de los casos "de novo" y en el 50% de los casos recidivantes.

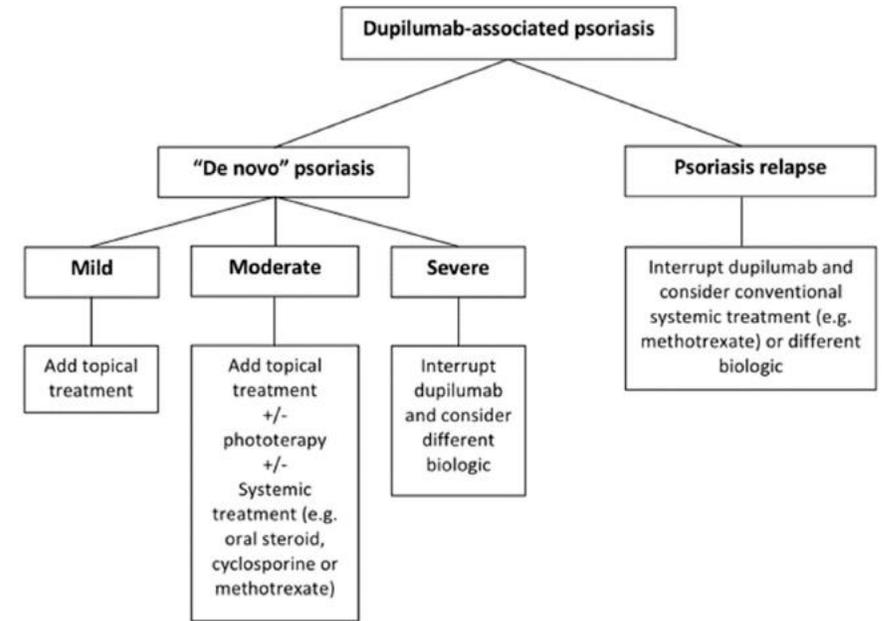


Figure 2. Proposed treatment algorithm for dupilumab-induced psoriasis.

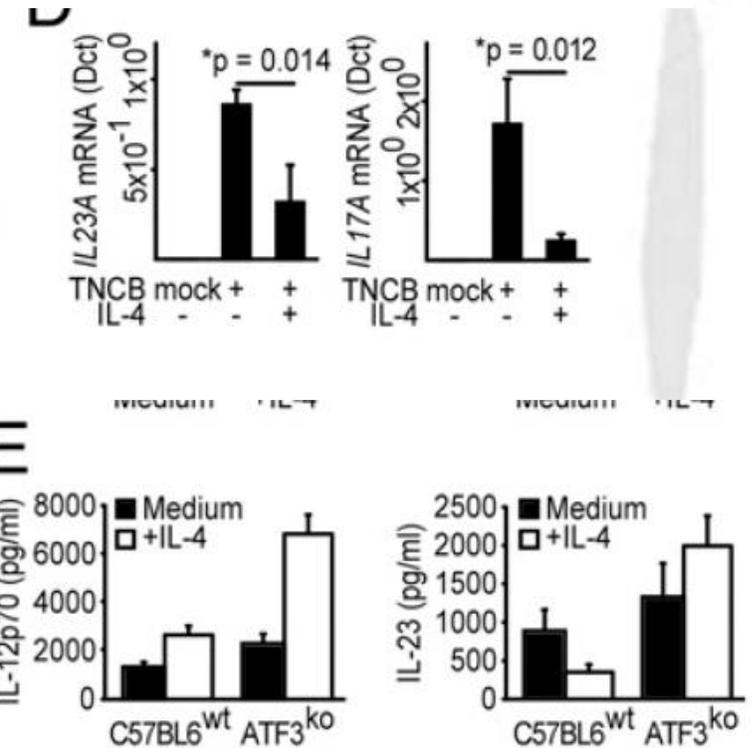
Review

"De Novo" Psoriasis and Relapse of Psoriasis Induced by Dupilumab: Three New Cases and Review of the Literature

Ilaria Trave, Ilaria Salvi , Martina Burlando , Emanuele Cozzani and Aurora Parodi

Reacciones psoriasiformes con terapias anti IL4

- La IL-4 promueve la producción de IL-12 por las células dendríticas (CD) y las células TH1 productoras de IFN- γ , pero inhibe la producción de IL-23.
- La IL-4 suprime los DTHR a través de la inhibición dependiente de STAT6 (transductor de señal y activador de la transcripción 6) de la IL-23 en las células presentadoras de antígenos.
- La terapia con IL-4 atenúa las DTHR al suprimir las respuestas de IL-23/TH17 a través de STAT6 y ATF3 (activando el factor de transcripción 3), al tiempo que mejora las respuestas de IL-12/TH1.



IL-4 abrogates T_H17 cell-mediated inflammation by selective silencing of IL-23 in antigen-presenting cells

Emmanuella Guenova^{a,b,c,1,2}, Yuliya Skabytska^{a,1}, Wolfram Hoetzenecker^{a,b,c,1}, Günther Weindl^{a,d}, Karin Sauer^a, Manuela Tham^a, Kyu-Won Kim^e, Ji-Hyeon Park^e, Ji Hae Seo^{e,f}, Desislava Ignatova^c, Antonio Cozzio^c, Mitchell P. Levesque^c, Thomas Volz^{a,g}, Martin Köberle^{a,g}, Susanne Kaesler^a, Peter Thomas^h, Reinhard Mailhammer^{i,3}, Kamran Ghoreschi^a, Knut Schäkel^l, Boyko Amarov^k, Martin Eichner^l, Martin Schaller^a, Rachael A. Clark^b, Martin Röcken^{a,2}, and Tilo Biedermann^{a,g,2}

www.pnas.org/cgi/doi/10.1073/pnas.1416922112

Reacciones psoriasiformes ... no solo terapias anti Il4

Paradoxical tralokinumab-induced psoriasis in a patient with atopic dermatitis

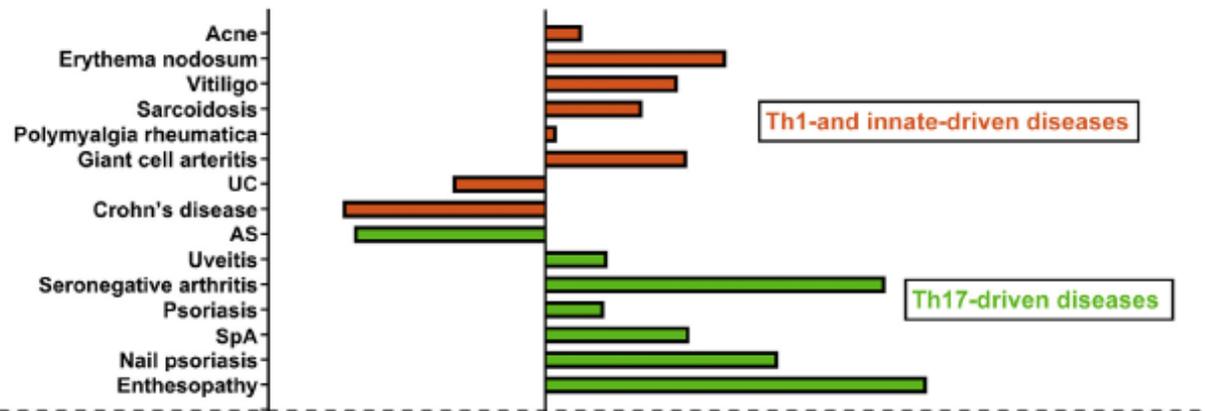
Galina Balakirski, Sven-Niklas Burmann, Silke C. Hofmann & Alexander Kreuter



Results: We present a 36-years-old male patient with a severe course of an intrinsic atopic dermatitis and dyshidrotic hand eczema. He responded well to the therapy with tralokinumab. However, about 7 months after the start of anti-IL-13 treatment the patient developed psoriasiform lesions. The drug was then discontinued. Currently, the patient is receiving topical therapy with topical corticosteroids and

No solo la psoriasis... también artritis seronegativa y entesitis/entesopatía

- Presencia de receptores de IL-4/IL-13 en tejidos blandos de la entesis.
- Las células T derivadas de la entesis producen niveles basales de IL-4.
- Papel protector de la IL-4/IL-13 en la inducción del eje IL-23-IL-17.



T Helper 2 IL-4/IL-13 Dual Blockade with Dupilumab Is Linked to Some Emergent T Helper 17–Type Diseases, Including Seronegative Arthritis and Entesitis/Entesopathy, but Not to Humoral Autoimmune Diseases

Charlie Bridgewood¹, Miriam Wittmann^{1,2,3}, Tom Macleod¹, Abdulla Watad^{1,4,5,6}, Darren Newton⁷, Kanchan Bhan⁸, Howard Amital^{4,5}, Giovanni Damiani^{9,10,11}, Sami Giryes^{1,12,13}, Nicola Luigi Bragazzi^{1,14} and Dennis McGonagle^{1,2}



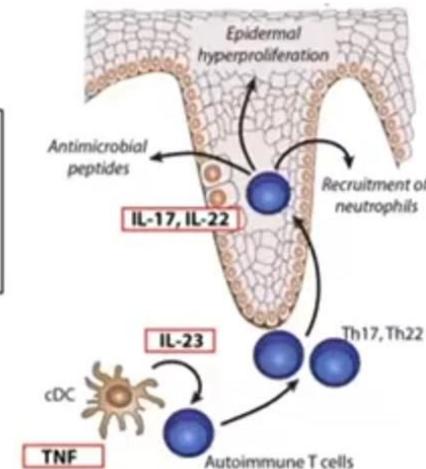
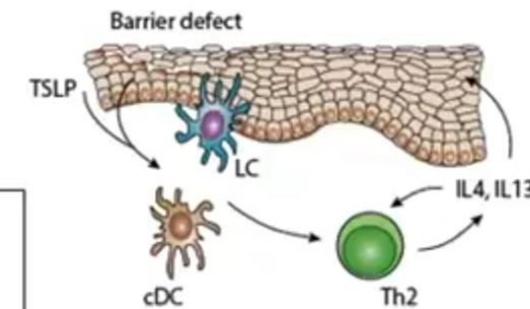
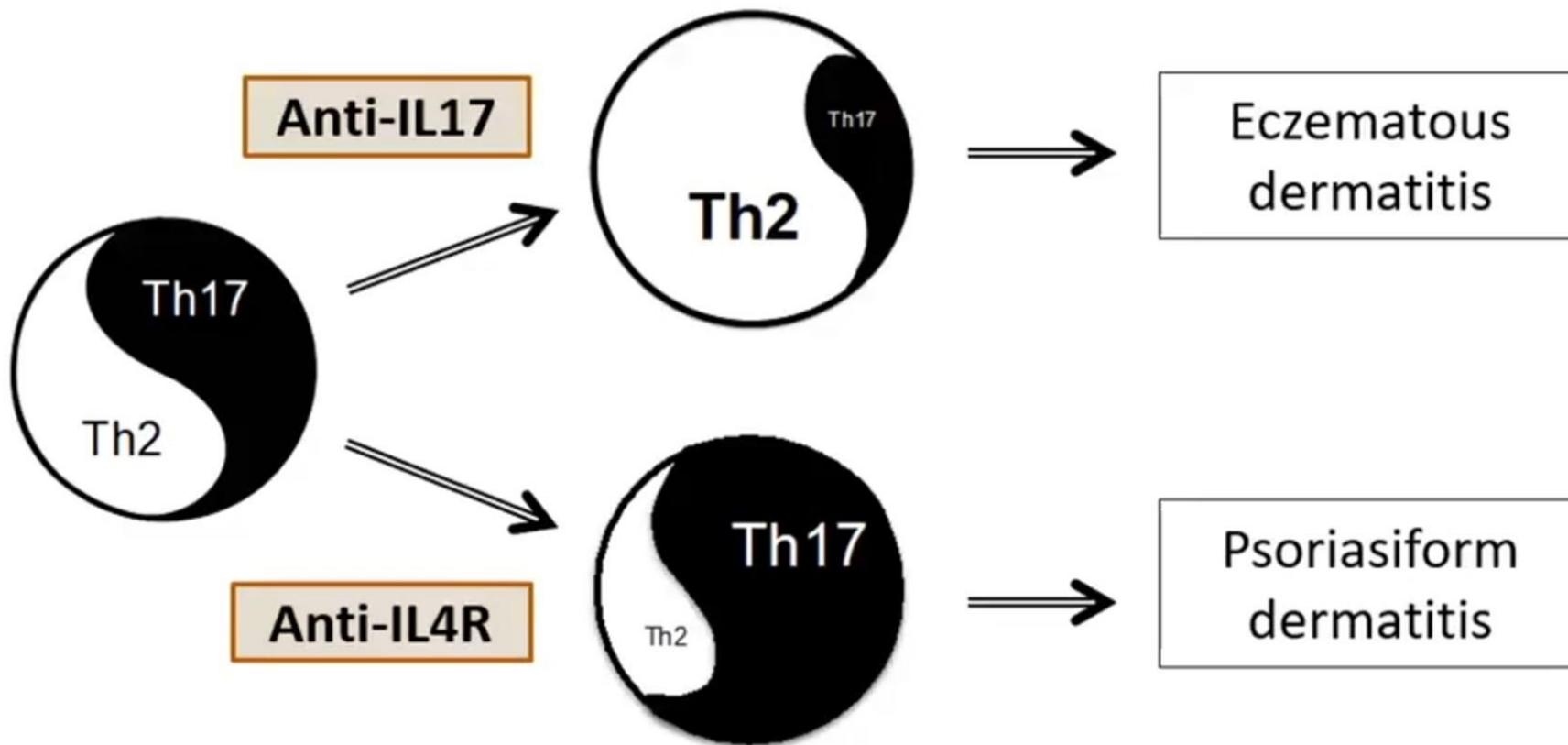
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The Yin-Yang of Th2/Th17



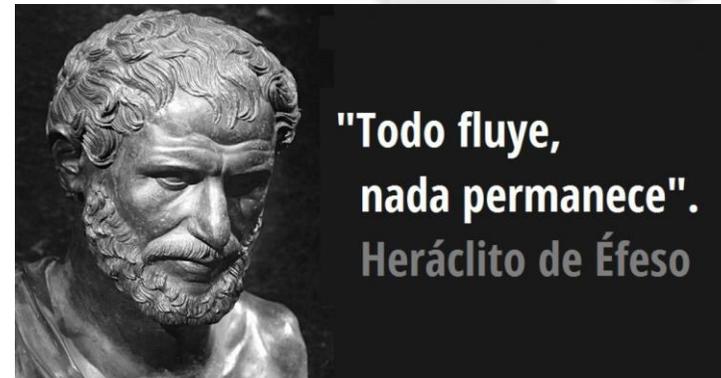
↑TSLP? barrier permeability?



↑IL-23? ↑CD11b^{high} DCs?



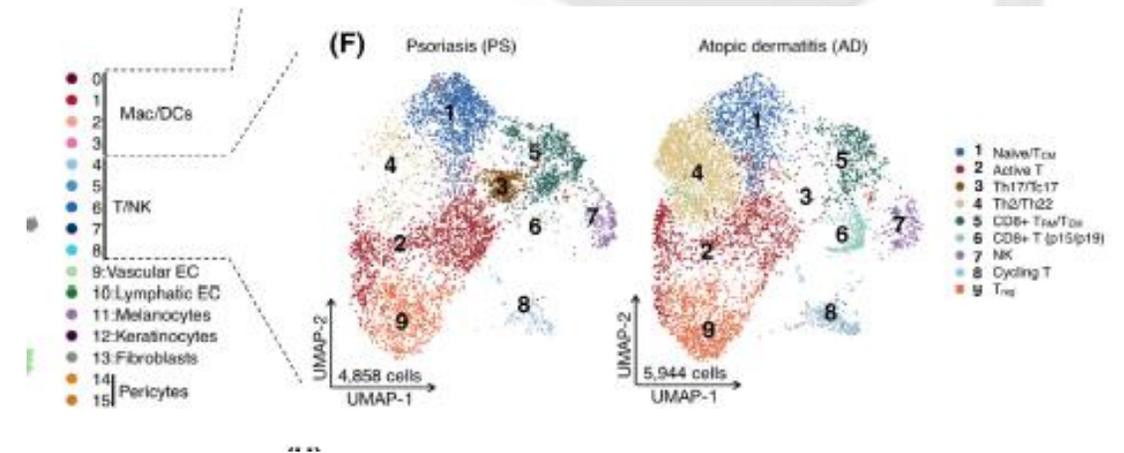
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@jmcarrascosa



"Todo fluye,
nada permanece".
Heráclito de Éfeso

Single-cell RNA en DD de Pso y AD

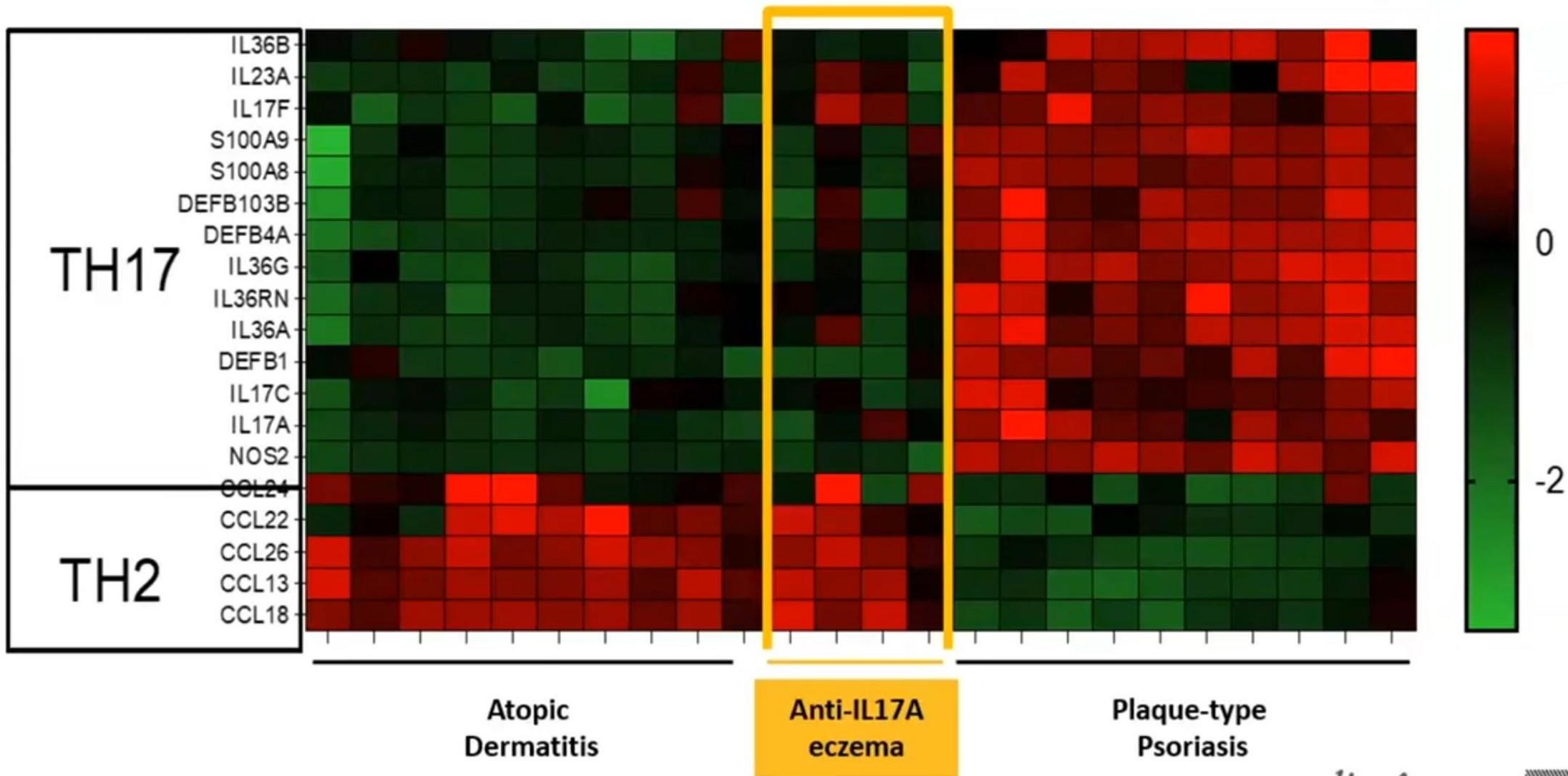
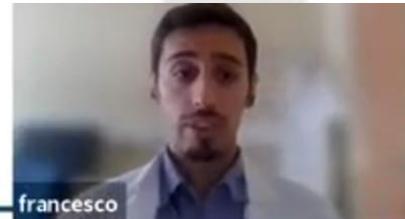
- Se utilizó la secuenciación de ARN de una sola célula y del receptor de células T (TCR) en células inmunitarias de biopsias de piel y muestras de sangre de pacientes con EA y PS.
- Las células T derivadas de la piel en ambas enfermedades mostraron TCR específico de la enfermedad, con patrones más pronunciados en PS.
- En AD, los grupos de células T fueron en su mayoría Th2/Th22
- En PS, fueron Th17/Tc17, correlacionándose con las puntuaciones de gravedad.



Single-cell profiles reveal distinctive immune response in atopic dermatitis in contrast to psoriasis

Bowen Zhang^{1,2} | Lennart M. Roesner^{3,4} | Stephan Traidl^{3,4} |
Valerie A. C. M. Koeken^{1,2,5} | Cheng-Jian Xu^{1,2,5} | Thomas Werfel^{3,4} | Yang Li^{1,2,4,5}

Anti-IL17A-induced Eczema shows T_H2 switch



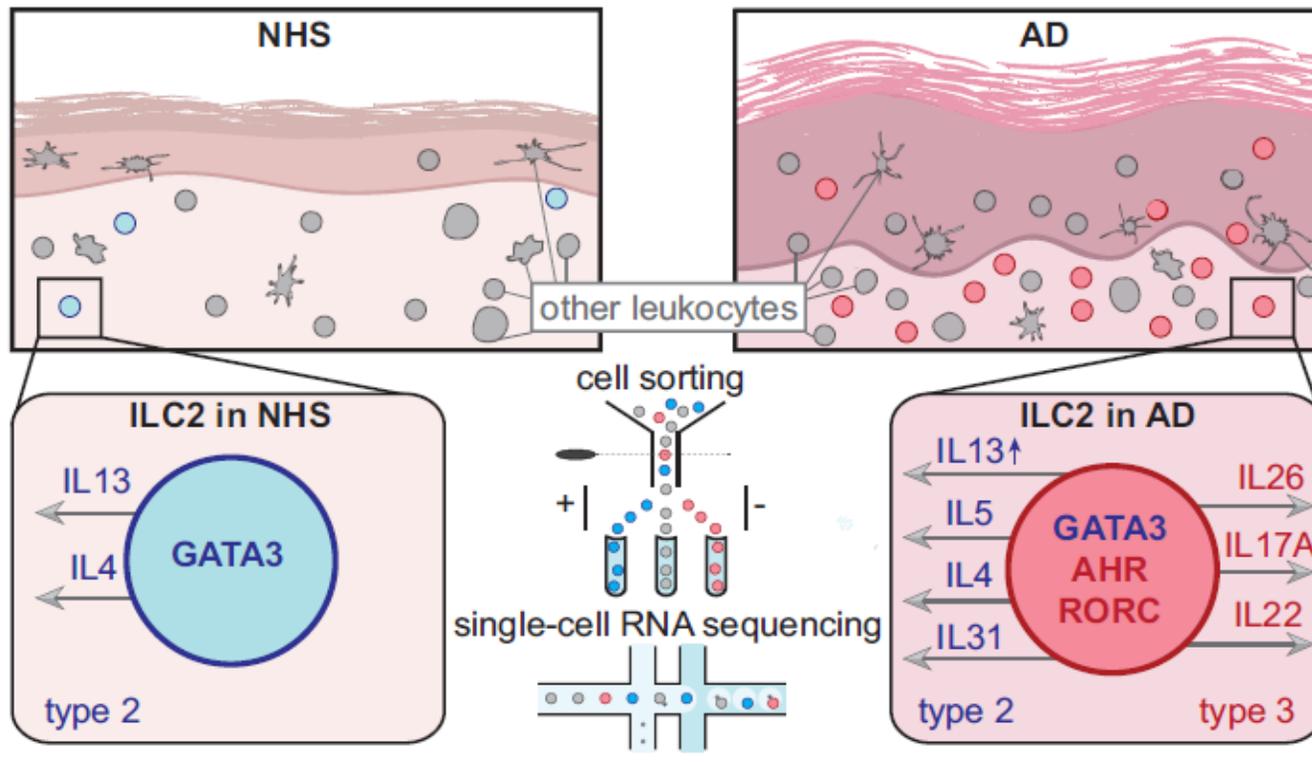
Single-cell analysis reveals innate lymphoid cell lineage infidelity in atopic dermatitis

Check for updates

Natalia Alkon, MSc,^{a*} Wolfgang M. Bauer, MD,^{a*} Thomas Krausgruber, PhD,^b Issac Goh, BSc,^c



Single-cell analysis reveals innate lymphoid cell lineage infidelity in atopic dermatitis



ILC-enriched cell samples confirmed the predominance of biologically heterogeneous group 2 ILCs and, for the first time, demonstrated considerable ILC lineage infidelity (coexpression of genes typical of either type 2 [*GATA3* and *IL13*] or type 3/17 [*RORC*, *IL22*, and *IL26*] immunity within individual cells) in

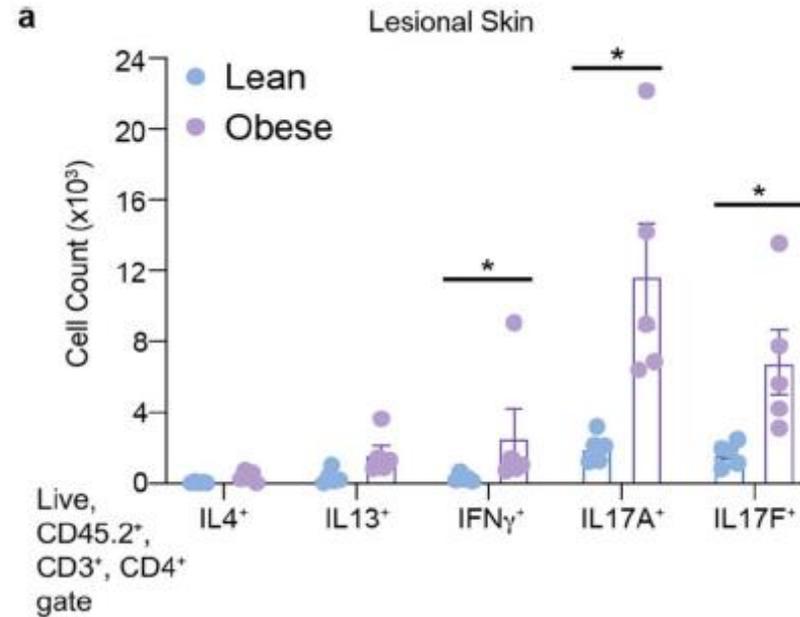
being a stable entity with well-defined components, the skin immune system consists of a network of highly flexible cellular players that are capable of adjusting their function to the needs and challenges of the environment. (J Allergy Clin Immunol

ILC2: type 2 Innate Lymphoid Cells; NHS: normal human skin; AD: atopic dermatitis; AHR: Aryl Hydrocarbon Receptor; RORC: RAR Related Orphan Receptor C



Hospital

La obesidad modifica la inflamación en la DA



Obesity converted the classical type 2 T helper (T_H2)-predominant disease associated with atopic dermatitis to a more severe disease with prominent T_H17 inflammation.

Single cell como método para distinguir entre "erupciones inespecíficas"

(hosted at <https://rashX.ucsf.edu>),

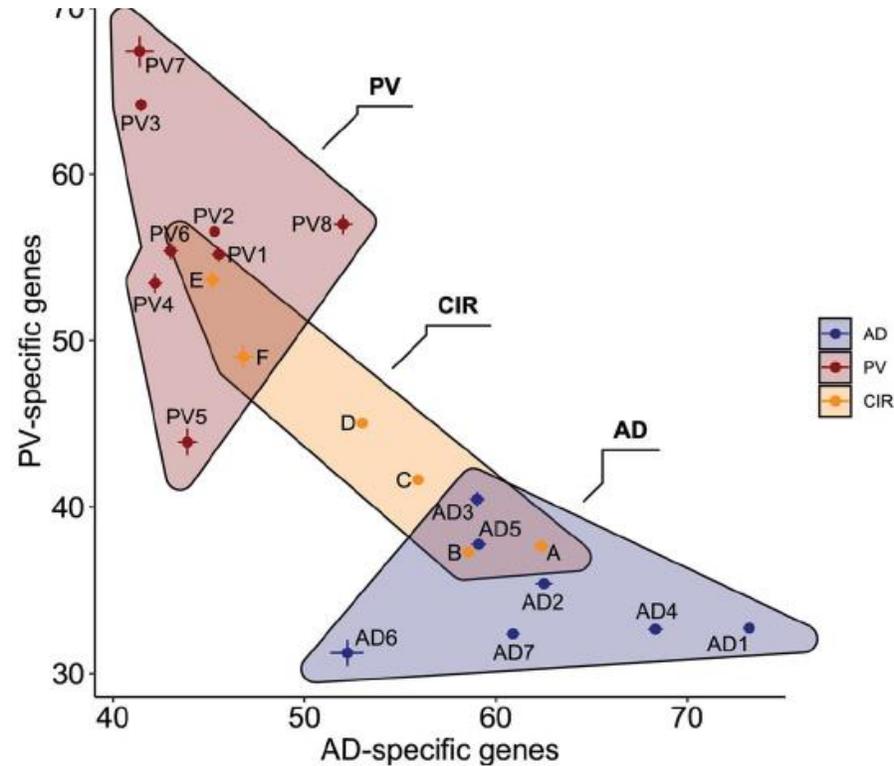


Fig. 6. Clinical/histopathologically Indeterminate Rashes (CIRs) show molecular stratification with atopic dermatitis or psoriasis-specific DEGs.

Compara tus resultados.....

← Back

Upload RDS file(s)

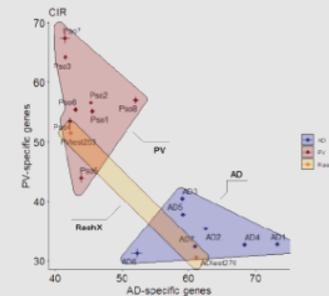
No file selected

Browse

Enter email address

Your email address

Submit



1. Upload patient scRNA-seq data matrix

* Download example atopic dermatitis and psoriasis vulgaris .rds files to upload and test in RashX

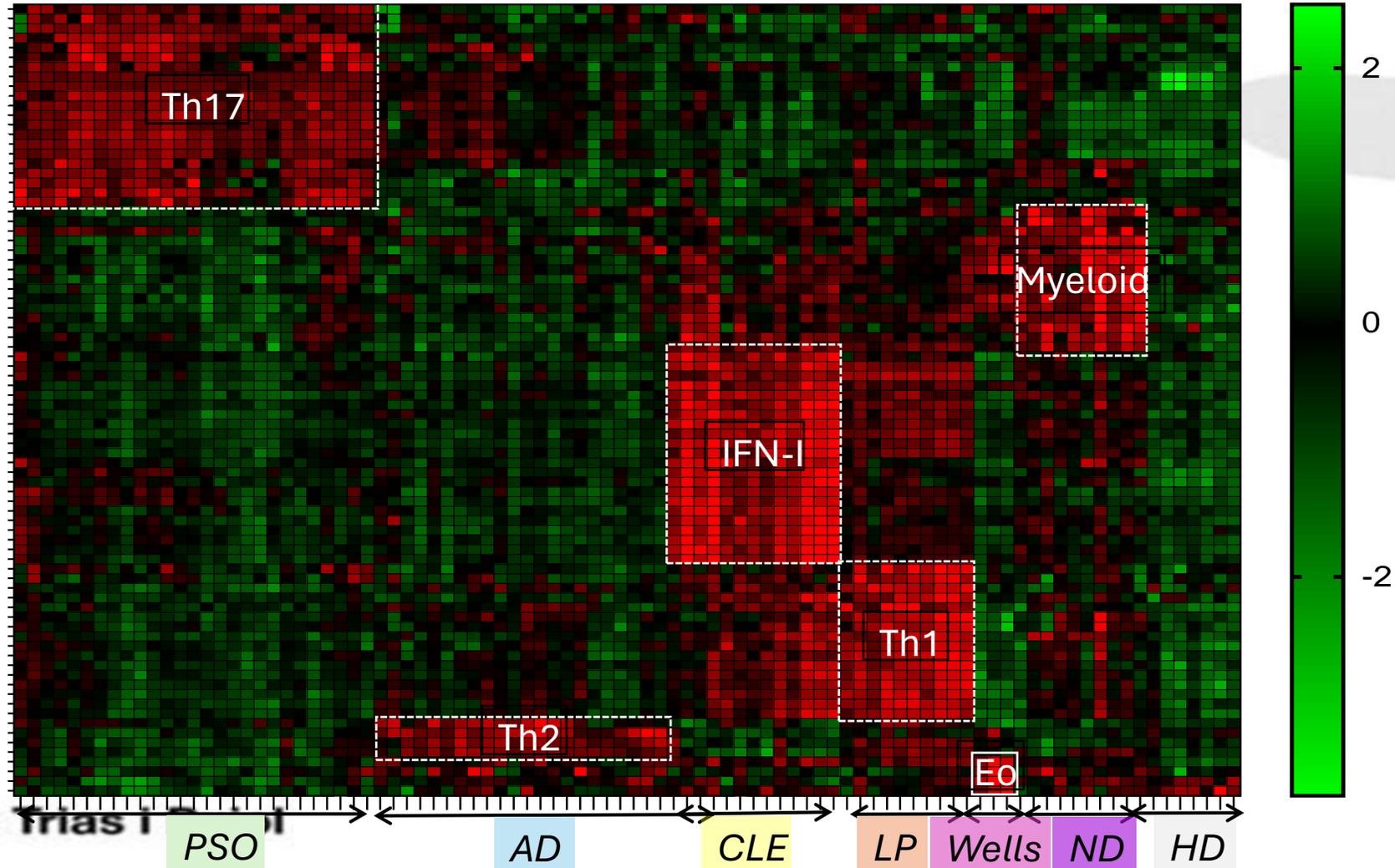
- [\(PV Sample\)](#)
- [\(AD Sample\)](#)

2. Allow 2-3 hours for algorithmic identification of skin-resident memory cells from sample matrix and RashX analysis

3. Receive an emailed, comparative visualization of uploaded sample in context of Liu et al atopic dermatitis and psoriasis vulgaris reference samples

hosted at <https://rashX.ucsf.edu>,

Molecular map of skin diseases



Overlapping Pso-AD

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- **Implicaciones terapéuticas**







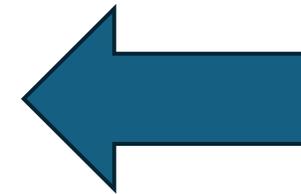
Variantes superpuestas de PSO-AD, implicaciones terapéuticas

Table 2. Reasonable choices for overlapping diseases.

| | Typical PSO | Typical AD | AD-PSO Overlapping |
|---------------------------------------|--|--|---------------------------------|
| Treatment | | | |
| Topical agents | Corticosteroids | Corticosteroids | Corticosteroids |
| | Vitamin D3 analog | Calcineurin inhibitor | |
| | Retinoids | PDE4 inhibitor (crisaborole) | Calcineurin inhibitor |
| | Tar | JAK inhibitor (ruxolitinib) | |
| | Calcineurin inhibitor * | | |
| Conventional oral medications | Methotrexate Acitretin Cyclosporin | Methotrexate * Azathioprine * Cyclosporin | Methotrexate Cyclosporin |
| Phototherapy | NBUVB # | NBUVB # | NBUVB # |
| Biologics | IL-12/23i, IL-17i, IL-23i, TNF- α i | IL-4/13i, IL-13i | IL-12/23i ? |
| Systemic small molecular drugs | PDE4 inhibitor (apremilast) JAK inhibitor (upadacitinib) ** | JAK inhibitor (baricitinib, upadacitinib, abrocitinib) | JAK inhibitor (upadacitinib) ** |

* Not licensed, but generally listed in worldwide treatment guidelines. # NBUVB: narrowband ultraviolet B.

? Well-tolerated but without efficacy in atopic dermatitis [93,94]. ** Licensed for psoriatic arthritis.



Germans Trias i Pujol

Int. J. Mol. Sci. **2022**, *23*, 5518. <https://doi.org/10.3390/ijms23105518>

Review

Overlapping Features of Psoriasis and Atopic Dermatitis: From Genetics to Immunopathogenesis to Phenotypes

Ya-Chu Tsai ¹ and Tsen-Fang Tsai ^{2,*} 

Abordaje terapéutico en la superposición de AD-Pso

- 4 patients treated with upadacitinib, at doses of 15 or 30mg, after unsuccessful results from standard treatments for both psoriasis and AD.
- Upadacitinib, a Janus Kinase 1 inhibitor, led to complete remission in these patients. It is currently approved for treating moderate-to-severe AD.
- A phase-3 trial for psoriatic arthritis showed 52.3% of patients achieving a 75% improvement PASI75 after one year on 15mg dose.

Table 1. Characteristics of our four patients with concomitant psoriasis and atopic dermatitis receiving upadacitinib.

| Patient N | Sex | Age | Psoriatic arthritis | Previous treatments | Upadacitinib dosage | Duration of follow-up (weeks) |
|-----------|-----|-----|---------------------|---|---------------------|-------------------------------|
| 1 | M | 12 | No | Ustekinumab, dupilumab | 15 mg | 52 |
| 2 | M | 39 | No | Cyclosporin, brodalumab | 15 mg | 36 |
| 3 | F | 50 | Yes | Salazopyrin, methotrexate, ustekinumab, secukinumab, apremilast | 15 mg | 32 |
| 4 | F | 42 | No | Adtretin, methotrexate, adalimumab, risankizumab, dupilumab | 30 mg | 60 |

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Upadacitinib for the treatment of concomitant psoriasis and atopic dermatitis: a case series

Luigi Gargiulo^{a,b}, Luciano Ibba^{a,b}, Giulia Pavia^{a,b}, Jessica Avagliano^b, Andrea Cortese^{a,b}, Antonio Costanzo^{a,b} and Alessandra Narcisi^b

Abordaje terapéutico en la superposición de AD-Pso

The patient was a 51-year-old woman with a 14-year history of PP psoriasis and refractory PsA, whose condition had shown little response to PUVA therapy, cyclosporin, azathioprine, ustekinumab, secukinumab, mycophenolate mofetil and adalimumab. Methotrexate, etanercept, apremilast and dimethyl fumarate had been discontinued due to intolerance

- Partial response with tofacitinib
- Complete response after 24 w of upadacitinib

Martinez-Molina M, Lluch-Galcerá JJ, Carrascosa JM. Response to upadacitinib in a patient with palmoplantar psoriasis. *Eur J Dermatol.* 2023 Jun 1;33(3):301-302. doi: 10.1684/ejd.2023.4489. PMID: 37594341.



Reacción similar a la psoriasis después de dupilumab tratado con JAKi



Reacción psoriasis-like después de dupilumab tratado con JAKi



W 4

Gracias por vuestra atención

**Somewhere, Something
Incredible Is Waiting To Be
Known.**

~ CARL SAGAN ~



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